it is shown that this assumption does not introduce any serious error within the limits of volume considered. We then find it possible to integrate the resulting differential equation, and the complete primitive enables us to draw a set of adiabatic curves. We believe that this is the first time adiabatic curves have been obtained for any substance except perfect gases.

A mathematical discussion is added as to what extent the equations

$$E = gT - h$$

and

$$g/b = \text{constant},$$

can be considered as strictly true, and not merely approximate.

The experimental results for liquid ether form an appendix to the paper.

"The Chemical and Physiological Reactions of certain Synthesised Proteid-like Substances. Preliminary Communication." By JOHN W. PICKERING, D.Sc. (Lond.). Communicated by Professor HALLIBURTON, F.R.S. Received November 10,—Read December 10, 1896.

The experiments of Professor Grimaux,* made more than ten years ago, have until recently attracted but little attention amongst English physiologists, although that investigator has synthesised a series of colloidal substances which, in their chemical characteristics, show striking similarities to proteids.

Working alone, and in collaboration with Professor Halliburton, I† have shown that three of the substances synthesised, viz., the "Colloids amidobenzoic A and B," formed by the interaction of phosphorus pentachloride and meta-amido-benzoic acid at 125° C., according to the details described in Grimaux's papers, and the "colloïde aspartique" formed by the passage of a current of dry gaseous ammonia over solid aspartic anhydride heated to 125° C., not only give the leading chemical reactions of proteids, but when intravenously injected into dogs, cats, or pigmented rabbits, cause extensive intravascular coagulation of the blood, in a manner indistinguishable from the physiological action of nucleo-proteids. When injected into the veins of albino rabbits or into the vascular system

* Grimaux, 'Comptes Rendus,' vol. 93, p. 771, 1881; *ibid.*, vol, 98, p. 105, 1884; *ibid.*, vol. 98, p. 1434 and p. 1578.

† Pickering, 'Journ. Physiol.,' vol. 14, p. 341, 1893; 'Comptes Rendus,' vol. 120, p. 1348, 1895; 'Physiol. Soc. Proc.,' Feb. 16, 1895 ('Journ. Physiol.,' vol. 17); 'Journ. Physiol.,' vol. 18, p. 54, 1895; *ibid.*, vol. 20, p. 171, 1896; *ibid.*, vol. 20, p. 310; Halliburton and Pickering, 'Journ. Physiol.,' vol. 18, p. 285, 1895.

of the Norway hare (*Lepus variabilis*), during its albino condition, these substances fail to induce intravascular coagulation of the blood, although they hasten the coagulation of the blood when drawn from the carotids, in a precisely similar manner to nucleo-proteids.

Taking these facts as the basis of my investigations, I have endeavoured to synthesise substances which will approach more nearly in their chemical and physiological reactions to proteids than those briefly described above; and to further investigate the properties of Grimaux's colloids.

I. *General Description of Experiments.*

I have up to the present synthesised seven different colloidal substances, by the interaction of either phosphorus pentachloride or pentoxide on certain well-known derivatives of proteids, and the details of their preparation, physical properties, chemical and physiological reactions are described below.

Colloid α.—Prepared by the interaction of equal parts of meta-amido-benzoic acid, biuret, and three times its weight of phosphorus pentoxide at 125° C. in a sealed tube. The best results are obtained by continuing the heating for about six hours, although a similar substance is obtained by heating for half an hour at 130° C. The product of the reaction is a pinkish-grey friable powder, which is insoluble in cold water, and almost insoluble in boiling water. This substance should be repeatedly washed until all traces of phosphoric acid are removed. When heated with Millon's reagent it fails to give the reaction characteristic of tyrosine and proteids; it also does not give the well-known colour reactions with the salts of copper, nickel, cobalt, and caustic potash. It gives the typical blue reaction associated with the name of Fröhde* when heated with sulphuric and molybdic acids, as well as the xantho-proteic reaction.

If the amount of biuret exceeds the amount of meta-amido-benzoic acid, then the excess of biuret left over gives its typical colour reaction with copper sulphate and potash.

The pinkish-grey powder, obtained by the reaction described above, should be dissolved in ammonium hydrate, and the resulting solution evaporated down at the temperature of the atmosphere *in vacuo*, when the resulting product appears as a number of translucent yellowish plates, which are tasteless and inodorous, and closely resemble in appearance both Grimaux's "colloïdes amido-benzoique and aspartique" and dried serum-albumen. These plates are with difficulty soluble in cold water, but readily pass into solution on warming. The solution obtained does not coagulate on heating, but

* Fröhde, 'Annalen der Chemie,' vol. 145, p. 376.

if a trace of a soluble salt of either barium, strontium, calcium, magnesium, or sodium be added, a pronounced coagulum is obtained on heating. This point will be returned to you in a subsequent section, but the similarity to dialysed serum-albumen may be pointed out, as that substance is stated not to coagulate when heated.*

The solution does not coagulate spontaneously on standing, neither will the addition of "fibrin ferment (*i.e.*, a nucleoproteid†) induce coagulation. It gives a typical xanthoproteic reaction, a violet with copper sulphate and potash, a dark heliotrope-purple with cobalt sulphate and potash, and a faint yellow with nickel sulphate and potash. It also gives Fröhde's sulpho-molybdic reaction; I may, however, remark that I found that several substances chemically allied to proteids yield this reaction, which is therefore not diagnostic of proteids alone. An alcoholic solution of alloxan gives with the solid plates a brilliant red coloration (Krasser's‡ reaction) similar to that produced with plates of serum-albumen. Negative results were obtained with the reactions associated with the names of Liebermann,§ Adamkiewicz,‖ and Millon.¶

The solution is neutral and lævorotatory ($\alpha_D = -52$), and if treated with pepsin and a 0·2 per cent. hydrochloric acid, or by an alkaline solution of trypsin, for several days at 38° C. it does not peptonise.

Qualitative analysis shows that this substance does not contain phosphorus in its molecule.

It is precipitated from solution by mercuric chloride, silver nitrate, and lead acetate. These precipitates yield the same colour reactions as the original substance.

The precipitate formed by the addition of lead acetate, like that obtained by the addition of this substance to a proteid solution, redissolves on the passage of a current of sulphuretted hydrogen through the solution in which it is suspended, and judging by chemical tests alone, the nature of the substance is unchanged by the processes of precipitation and redissolving. Its physiological action is, however, markedly changed, as will be shown later on.

The original solution is readily precipitated by trichloracetic, phosphotungstic, phosphomolybdic acids, and by acetic acid and potassium ferrocyanide, as well as by salicylsulphonic acid; the precipitate formed by this last substance is coagulated by heating in a manner similar to the coagulation produced by heating the precipitate resulting from the addition of this substance to a proteid

* Schmidt and Aronstein, 'Pflüger's Archiv,' vol. 8, p. 75, 1874.

† *Vide* Halliburton, 'Journ. Physiol.,' vol. 18, p. 306, 1895.

‡ Krasser, 'Monat. für Chem.,' vol. 7, p. 673; 'Maly's Jahresb.,' vol. 16, p. 1.

§ Liebermann, 'Maly's Jahres.,' vol. 18, p. 8.

‖ Adamkiewicz, 'Ber. d. deut. Chem. Gesell.,' vol. 8, p. 761.

¶ Millon, 'Comptes Rendus,' vol. 28, p. 40.

solution. I may here mention that salicylsulphonic acid does not precipitate disintegration products of proteids like leucine, tyrosine, xanthine, or hypoxanthine.

All the precipitates cited above give the colour reactions characteristic of the original substance.

If the original solution is saturated with either magnesium sulphate, ammonium sulphate, or sodium chloride, the whole of the colloid rises to the surface of the liquid, and may be skimmed off. On placing this scum in an excess of distilled water, it rapidly redissolves, forming a pale yellow opalescent solution, which gives all the chemical reactions characteristic of the original substance. If the amount of neutral salt be insufficient to produce precipitation, the passage through the liquid of a current of carbon dioxide or of sulphur dioxide will effect the same result. Neither of these gases will, however, cause precipitation in the entire absence of salts.

The following experiments illustrate the results produced by the intravenous injection of this substance into dogs, rabbits, and cats. The procedure adopted was identical with that described in the previous papers published by Professor Halliburton and myself,* on the intravascular injection of Grimaux's colloids. In all cases the animal was anæsthetised by a mixture of chloroform and ether, an excess of the latter substance being used when the subjects were dogs.

Experiment 1.—Fox terrier (weight 27 lbs. 10 oz.); 25 c.c. of a 0·75 per cent. solution of the colloid α was injected, and proved fatal. Pronounced exophthalmos and dilatation of the pupils, and typical stretching movements were observed.

Post-mortem examination made immediately after death revealed pronounced clots in the jugular vein, inferior vena cava, and portal vein, and a slight clot in the left ventricle and in the pulmonary artery.

Experiment 2.—Large black cat (weight 9 lbs. 6 oz.); 40 c.c. of the colloid proved fatal, with similar symptoms as above. Immediate *post-mortem* examination showed pronounced clots in the left ventricle, right auricle, inferior vena cava, portal, and jugular veins. The remainder of the blood was fluid, but coagulated very rapidly after withdrawal.

Experiment 3.—Black rabbit; 38 c.c. of the same substance produced a similar result.

Experiment 4.—Albino rabbit; 42 c.c. proved fatal. Death was accompanied by pronounced exophthalmos and dilatation of the pupils and stretching movements of the limbs. *Post-mortem* examination showed the blood throughout the vessels to be fluid. It, however, rapidly coagulated after withdrawal from the vessels, and the coagulability of samples of the blood taken from the carotids during

* *Op. cit.*

the injection of the colloid was also hastened; thus after 20 c.c. of the colloid had been injected, the time of complete coagulation of blood withdrawn from the carotids was hastened by 2 minutes, after 30 c.c. by $3\frac{1}{2}$ minutes, and after 35 c.c. by 4 minutes.

It will be evident that the results recorded above are similar to, if not indistinguishable from, those produced by the intravenous injection of a nucleoproteid.

When slowly introduced into the circulation of dogs, and to a much lesser degree of rabbits, in minute quantities, the effect produced on the coagulability of the blood is the converse of that resulting from the introduction of larger quantities. This effect is more pronounced than that obtained by the intravenous injection of Grimaux's colloids, and more resembles Wooldridge's* "negative phase," which is characteristic of a nucleoproteid, but is not so pronounced as the result obtained with that substance.

This result is illustrated by the following experiment:—

Experiment 5.—Large black mongrel. Anæsthetic, ether and morphia (weight, 60 lbs.); 1 c.c. of a 0·025 per cent. solution colloid α was injected very slowly, the injection being distributed over half an hour, at the end of which time the retardation of the time of coagulation of blood withdrawn from the animal's carotid was found to be 8 minutes 30 seconds. A second dose of 1 c.c. of the same solution injected and distributed over 20 minutes caused a further retardation in the time of coagulation of the carotid blood of 2 minutes; but a third injection distributed over a similar period of time hastened the coagulability of the blood that had been previously retarded, so that the retardation, as compared with the time of coagulation before the injection of the colloid, was only 1 minute 30 seconds. After a still further injection of the colloid, the blood coagulated more rapidly than in the normal condition, and finally, when the dose was pushed, intravascular coagulation of the animal's blood occurred, and death resulted.

If the colloid is separated from the solution by saturation with magnesium sulphate, sodium chloride, or ammonium sulphate, as before described, and the scum redissolved in distilled water, the opalescent solution obtained will, when intravenously injected into pigmented rabbits, produce typical intravascular coagulation. Repetition of the process of precipitation and redissolving however, destroys the physiological activity in a manner similar to the result produced with both nucleo-proteids and Grimaux's synthesised colloids.

If the solution formed by the passage of a stream of sulphuretted hydrogen over the precipitate formed by the addition of lead acetate to the colloid is injected intravenously into pigmented rabbits or

* Wooldridge, 'Du Bois-Reymond's Archiv,' 1886, p. 397; 'Proc. Roy. Soc.,' vol. 40, p. 134, 1886.

dogs, it is found not to induce intravascular coagulation, although its chemical and physical characteristics are apparently unchanged. This result shows that the chemical reactions used for "testing" proteids are not sufficiently delicate to indicate the chemical changes which are demonstrable by physiological methods. The following experiment illustrates this result:—

Experiment 6.—Black rabbit (weight 7 lbs. 9 ozs.); anæsthetic, chloroform and ether; 120 c.c. of redissolved solution injected produced dyspnœa, exophthalmos, dilatation of pupils. A further injection of 10 c.c. of this substance was immediately fatal. *Post-mortem* examination failed to reveal any clots in the animal's vessels. Blood withdrawn from the carotids during the injection showed only one minute's decrease in the time taken to complete coagulation.

Experiment 7.—In another experiment, where minute quantities of this substance were very slowly injected, there was no retardation of the time of coagulation, like that produced by the original substance or by a nucleo-proteid.

Colloid β.—This substance is formed by heating together tyrosine, biuret, and phosphorus pentachloride in the ratio of equal weights of the two former substances, with twice the weight of the latter, for six hours at 125° to 130° C. in sealed tubes. The product of this reaction is a grey powder insoluble in cold water, and very sparingly soluble on heating. This substance gives the xantho-proteic and Fröhde's reaction, but fails to give typical colour reactions with the other reagents commonly used in testing proteids. It should be repeatedly washed until all traces of the contaminating phosphoric acid are removed, and then dried *in vacuo* at about 30° C. It readily dissolves in concentrated ammonium hydrate, and the solution is opalescent and lævorotatory ($\alpha_D = -48$), and in appearance indistinguishable from that of the other colloids produced. It gives the following distinctive reactions as classified in the annexed table, but does not digest when subjected to the action of either pepsin and 0·2 per cent. hydrochloric acid for three days at 38° C., or of an alkaline solution of trypsin, kept at the same temperature for a similar time. It yields the following distinctive reactions:—

Colloid β.

$CuSO_4$ KHO.	$CoSO_4$ KHO.	$NiSO_4$ KHO.	H_2SO_4 and molybdic acid.	Millon's reagent.	HNO_3 and NH_4OH (heating).	Salicyl sulphonic acid.
Violet-coloured solution.	Heliotrope purple-coloured solution.	Faint yellow-coloured solution.	Dark blue precipitate.	Dark red precipitate.	Orange precipitate.	Precipitate which coagulates on heating.

It gives negative results with the reactions of Liebermann and Adamkiewicz, but gives the typical red coloration when the solid plates are heated with an alcoholic solution of alloxan (Krasser's reaction). It is separated from solution by neutral salts in a manner similar to the colloid α and Grimaux's colloids. The scum also redissolves in distilled water giving an opalescent straw-coloured solution. It is precipitated by silver nitrate, lead acetate, and mercuric chloride, as well as by phosphotungstic, phosphomolybdic, and trichloracetic acids, and by acetic acid and potassium ferrocyanide.

In the entire absence of salts it is not coagulated on boiling, but, on the addition of a trace of a soluble salt of either sodium, magnesium, barium, strontium, or calcium, a coagulum is obtained on heating to 74° C.

The fractional heat coagulation of this substance will be dealt with in a subsequent section.

The effect produced by the intravascular injection of various quantities of this body is illustrated by the following experiment:—

Experiment 8.—Brown mongrel (weight 27 lbs. 7 oz.); anæsthetised with ether and morphia. The jugular vein on the one side, and the carotid artery on the other, were exposed, and cannulæ inserted into them. The colloid β was injected into the jugular vein, and samples of blood withdrawn from the artery. The following table shows the rate of clotting of the various samples:—

(1) Before injection of the colloid, the blood clotted in 10 minutes 30 seconds.
(2) 5 c.c. of 0·75 per cent. solution of colloid dissolved in 0·75 per cent. saline injected. A firm clot formed in 17 minutes 8 seconds.
(3) 10 c.c. more injected. Loose clot in 22 minutes.
(4) 10 c.c. more injected. Firm clot in 31 minutes.
(5) 10 c.c. more injected. Firm clot in 13 minutes.
(6) After interval of 5 minutes a second sample of carotid blood formed a firm clot in 7 minutes 30 seconds.
(7) 7 c.c. more injected. Firm clot in 7 minutes 30 seconds.
(8) 10 c.c. more injected. Firm clot in 6 minutes.
(9) 15 c.c. more injected. Firm clot in 3 minutes.
(10) 10 c.c. more injected and proved fatal.

Immediate *post-mortem* examination revealed loose clots in vena cava inferior, and jugular vein, and pronounced clots in portal vein, and right ventricle.

This experiment shows the "negative phase" after injection of small quantities of the colloid β, and the typical hastening of the coagulability of the blood withdrawn from the carotid after the intravenous injection of

a larger dose, and finally the coagulation of the intravascular blood when the dose is again increased.

Colloid γ.—The colloid γ is formed by heating together at 130° C. in sealed tubes, for three hours equal weights of alloxan and metamidobenzoic acid, with twice their weight of phosphorus pentoxide. The product of the reaction is a white powder, very slightly soluble in cold water, and sparing soluble in warm water. It should be washed in ice-cold water till the excess of phosphoric acid is removed, and the remaining substance dissolved in concentrated ammonia. The resulting solution is opalescent and straw-coloured, and should be evaporated down at the temperature of the laboratory *in vacuo*, when a number of translucent, yellowish plates, closely resembling the previously described colloids are formed. These plates are soluble in warm water, and the solution is pale straw-coloured, opalescent, and lævorotatory ($\alpha_D = -41$) and shows the following reactions:—

Colloid γ.

HNO_3 NH_4OH. (heating).	Millon's reagent.	Fröhde's reaction.	$CuSO_4$ and KHO.	$NiSO_4$ and KHO.	$CoSO_4$ and KHO.	Salicyl-sulphonic acid.
Yellow solution.	Dirty brown ppt.	Blue precipitate.	Violet solution.	Very faint yellow solution.	Dark brown solution.	No precipitate.

It is separated from solution by saturation with either magnesium sulphate, sodium sulphate, sodium chloride, or ammonium sulphate, the colloid rising to the surface of the liquid as a white scum, which redissolves, forming an opalescent solution when thrown into distilled water. It is precipitated by silver nitrate, lead acetate, and mercuric chloride. If the precipitate formed by the addition of lead acetate is suspended in distilled water, and a current of sulphuretted hydrogen is passed through the liquid, the precipitated colloid again passes into solution.

When heated in the presence of a trace of a neutral salt, fractional heat-coagulation is obtained, which will be detailed in a subsequent section.

If the colloid γ is injected into the circulation of dogs or pigmented rabbits, even in large quantities, it does not produce intravascular coagulation, although it somewhat hastens the coagulability of blood withdrawn from the carotid.

The colloid γ, although yielding many of the chemical reactions that have been used as distinctive tests for proteids, and also behaving in a very similar manner to the previously described proteid-like colloids, does

not, like them, produce intravascular coagulation when intravenously injected into pigmented rabbits. Neither will the colloid γ when introduced into the circulation of dogs, very slowly and in minute quantities, produce a retardation of the coagulation of blood withdrawn from the carotids.

Colloid δ.—The colloid δ is formed by heating at 125° C. in sealed tubes for three hours, equal weights of para-amidobenzoic acid and phosphorus pentachloride. The resulting product, a grey friable powder, insoluble in cold water, was, after washing to remove the contaminating phosphoric acid, dissolved in concentrated ammonia, and evaporated down at a low temperature *in vacuo*. The resulting substance appears as a number of translucent yellowish plates, apparently similar to those previously described. They are soluble in warm water, forming an opalescent straw-coloured solution, which is lævorotatory ($\alpha_D = -42$). This solution gives the xantho-proteic and Fröhde's reaction, but fails to give the typical colour reactions of proteid-like substances with salts of copper, cobalt, or nickel and caustic potash; neither does it give the reactions of Millon, Liebermann, or Adamkiewicz. It is not precipitated by salicylsulphonic acid, but it is precipitated by salts of the heavy metals. Neutral salts separate it from solution like the preceding substances. When freed from salts, it does not coagulate on heating, but if a trace of sodium chloride or of another neutral salt be present, it coagulates on heating to 75° C. When intravenously injected into pigmented rabbits, it fails to produce intravascular coagulation, neither does it hasten the coagulability of blood withdrawn from the carotids. It fails to induce a "negative phase" in the coagulation of dogs' blood. This series of results lends additional support to the view that the coagulation of the blood resulting from intravenous injection of the colloid, is due to the interaction of the colloid with the constituents of the plasma, and not to the heavy nature of colloid molecule.

Colloid ϵ.—The colloid ϵ is prepared by heating together equal weights of tyrosine and xanthine with twice their weight of phosphorus pentachloride at 125° C. for three hours. The product of the reaction is a yellowish powder slightly soluble in warm water. After repeated washing in cold water, it is dissolved in concentrated ammonia, and the resulting solution evaporated down *in vacuo* at a low temperature. The resulting substance consists of a number of translucent yellowish plates like those previously described. It is readily soluble in warm water, forming a yellowish opalescent solution, which is lævorotatory ($\alpha_D = -38$).

This solution gives a typical red when heated with Millon's reagent, which is not due to an excess of tyrosine, since the intermediate product in the preparation of the substance fails to give this reaction. It does not give any other of the distinctive proteid colour reactions,

but is precipitated by salicylsulphonic acid, and the precipitate coagulates on heating. It behaves with neutral salts and salts of the heavy metals similarly to the previously described substances. It does not cause intravascular coagulation of the blood when intravenously injected into dogs or pigmented rabbits, neither will the very slow injection of minute quantities into the circulation of dogs induce a "negative phase." It does not induce coagulation when added to 1 per cent. sodium carbonate plasma.

Colloid ζ is prepared in a similar manner to the colloid ϵ, hypoxanthine being substituted for xanthine. It has a similar appearance to the colloid ϵ, is lævorotatory ($\alpha_D = -40$), gives Millon's reaction, and negative results with the other tests characteristic of proteids.

It also behaves with neutral salts and salts of the heavy metals in a similar manner to the previously described substances. When intravenously injected into the circulation of dogs or pigmented rabbits, it fails to induce intravascular coagulation, neither will it cause coagulation when added to extravascular 1 per cent. sodium carbonate plasma.

Colloid η.—The colloid η is prepared by the interaction of tyrosine and phosphorus pentoxide for three hours at 130° C. in sealed tubes. The product of this reaction is a pinkish friable powder, sparingly soluble in cold water and soluble on boiling. This substance does not yield Millon's reaction. After washing in cold water to remove the contaminating phosphoric acid, the powder is dissolved in concentrated ammonia, and a straw-coloured opalescent solution is obtained. This is evaporated down *in vacuo*, and the resulting substance appears as a number of plates, similar in appearance to those of the previously described colloids, and which are soluble in warm water, giving an opalescent solution. This solution is precipitated by salicylsulphonic acid and the precipitate coagulates on heating. It is also precipitated by salts of the heavy metals, and separated from solution by neutral salts. It does not yield any of the distinctive colour reactions of proteids, and fails to produce intravascular coagulation when intravenously injected into rabbits.

II. *The Fractional Heat Coagulation of Synthesised Colloids.*

The method of differentiating the members of a mixture of proteids by fractional heat coagulation was introduced by Halliburton,* and employed by him more especially in the examination of the proteids of serum. This method was subsequently used by Corin and Bérard† in separating the albumins of the white of egg, and by Chittenden

* Halliburton, 'Journ. Physiol.,' vol. 5, p. 159.

† Corin and Bérard, 'Bul. de l'Acad. Roy. de Belgique,' vol. 15, 4, 1888.

and Osborne* in studying the proteids of maize. The method was rendered more accurate by Hewlett,† who substituted a bath of cod-liver oil for the water bath usually employed as the heating medium, and exhaustively dealt with the adverse criticisms made by Haycraft and Duggan.‡

I have applied this method, using an oil bath, in the examination of the proteid like colloids synthesised by Professor Grimaux and myself. As pointed out in a previous section, in the entire absence of salts these substances do not coagulate, even when boiled. For the sake of comparison the following experiments were performed, so as to satisfy the following conditions:—(*a*) A 2 per cent. solution of the substance under examination was always used. (*b*) The diluent fluid always consisted of a 0·75 per cent. solution of sodium chloride. (*c*) In each experiment 10 c.c of the fluid under examination was used, and the test-tubes were of uniform internal diameter. By this means the mass to be heated remained constant. (*d*) The thermometer was placed in the middle of the test-tube containing the fluid under examination.

The colloid A ("colloïde amidobenzoique" of Grimaux) shows a coagulation temperature of 70° to 71° C.

The colloid B (of Grimaux) which is prepared from the same reagents as the colloid A, but the temperature at which the reaction of synthesis is conducted is allowed to rise to 130° C., shows on heating one faint appearance of flocculi at 56° to 58° C., and a second more pronounced coagulum at 70° to 72° C.

The colloid C ("colloïde aspartique" of Grimaux) on fractional heating shows three distinct sets of flocculi, appearing respectively at 58°, 67°, and 73·1° to 76·4° C.

The colloid α, if care has been taken to keep the temperature of preparation constant at 125° C., shows, on heating, only one coagulum at 70·6°; if, however, in the preparation of this colloid the temperature of synthesis is allowed to rise, a second colloid coagulating at 42° C. is often but not always formed.

The colloid β, even when the temperature of the synthesis has been kept constant at 130° C., shows, on heating, three constituents coagulating at 47° C., 56° C., and 74° C.

The colloid γ apparently only has one temperature of heat coagulation, viz., 75° C.

The colloid δ coagulates at 75° C.

The colloid ϵ coagulates only at 47° C.

The colloid ζ coagulates at 48° and 59° C.

* Chittenden and Osborne, 'Amer. Chem. Journ.' vol. 13, 7 and 8; vol. 14, 1.

† Hewlett, 'Journ. Physiol.,' vol. 13, p. 493, 1892.

‡ Haycraft and Duggan, 'Brit. Med. Journ.,' 1890, vol. 1, p. 167; 'Edin. Roy. Soc. Proc.,' vol. 16, p. 361, 1888–9.

The colloid η coagulates only at 52° C.

Adopting the conclusion of Halliburton that the precipitates obtained by the fractional heat coagulation of a proteid substance, correspond with various constituents of that substance, we may possibly conclude that those synthesised colloids which yield fractional heat-coagula are mixtures of different colloidal substances.

Thus the colloid B would consist of two substances which might be designated B_1 and B_2, and the colloid β of three substances, designated colloids β_1, β_2, and β_3 respectively, and the colloid ϵ of two substances, ϵ_1 and ϵ_2. I have endeavoured to ascertain in the cases of the colloids B_1 and B_2 and of the colloids β_1, β_2, and β_3 whether each of these substances will equally induce intravascular coagulation of the blood, when intravenously injected into pigmented rabbits and dogs.

The method of procedure adopted was briefly as follows:—The activity of a solution of the colloid was tested by a control experiment. One of the constituents was removed by fractional heat-coagulation and the effect, if any, produced by the intravascular injection of the remaining colloid in solution was tested.* The following is the record of some of the results obtained:—

Colloid B_2 after a removal of colloid B_1 will, if intravenously injected, induce intravascular coagulation in pigmented rabbits, and if slowly injected in minute doses a "negative phase" in dogs.

Colloids β_2 and β_3 will still, after the removal of colloid β_1, induce intravascular coagulation in pigmented rabbits, although a much larger dose is required after the removal of β_1 and β_2 than if the mixture of the three substances is injected, if only β_1 is removed the activity of the mixture is not impaired. From this I conclude that β_2 and β_3 are the active constituents of the colloid mixture I have designated as the colloid β. There is apparently no difference in the tendency to induce a "negative phase" in dog's blood after the removal of β_1 and β_2 from the solution.

III. *Other Properties of the Synthesised Colloids.*

The influence of these substances on red and white blood corpuscles, and on extravascular 1 per cent. sodium carbonate plasma will be described in a subsequent paper.

IV. *Concluding Remarks.*

It is evident from the observations recorded in the preceding pages, that if certain derivatives of proteids, and other substances of

* The solution after removal of one of its constituents by fractional heat-coagulation, was evaporated down *in vacuo* until it had the same specific gravity as the original solution.

allied chemical constitution are heated together in sealed tubes with an excess of either phosphorus pentachloride or pentoxide, a series of colloidal substances are formed which, when freed from the contaminating phosphoric acid, and dissolved in concentrated ammonia, give opalescent solutions that, on evaporating down *in vacuo*, yield substances closely resembling in physical, chemical, and physiological properties certain proteids.

These colloidal substances, although they differ from one another in minor details, are usually distinguished by the following characteristics :—

1. They are soluble in warm water, forming opalescent lævorotatory solutions.

2. The resulting solutions yield the principal colour reactions hitherto deemed diagnostic of proteids.

3. In the absence of salts, solutions of these colloids do not coagulate on heating. In the presence of a trace of a neutral salt they coagulate on heating at temperatures very similar to proteid solutions.

4. Fractional heat-coagulation shows the colloidal solutions are a mixture of different substances.

5. The different constituents of the colloidal solution exhibit different physiological action.

6. In the presence of an excess of neutral salts, or of salts of the heavy metals, the colloidal solutions behave in a manner similar to proteid solutions.

7. When introduced into the circulation of pigmented rabbits, dogs, and cats, certain of these substances (viz., the colloids designated A, B, C, α and β) produce intravascular coagulation of the blood in a manner similar to a nucleo-proteid. They also hasten the coagulability of the blood withdrawn from the carotid, and will, when slowly injected intravenously in minute quantities into dogs, produce a retardation of the coagulability of the intravascular blood, *e.g.*, a "negative phase."

8. Apparently these colloidal substances are, owing to both their physical and chemical properties and their physiological behaviour, the nearest synthesised bodies at present known to proteids.

"An Experimental Examination into the Growth of the Blastoderm of the Chick." By RICHARD ASSHETON, M.A. Communicated by ADAM SEDGWICK, F.R.S. Received November 12,—Read December 10, 1896.

In making an experimental study of the growth of the blastoderm of the chick, I had two chief objects in view :